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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,508	09/22/2000	Henry E. Young	1304-1-019CIP	1973

7590

01/12/2006

David A Jackson Esq  
Klauber & Jackson  
411 Hackensack Avenue  
Hackensack, NJ 07601

EXAMINER

TON, THAIAN N

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/668,508

Applicant(s)

YOUNG ET AL.

Examiner

Thaian N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 14-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 September 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/05 has been entered.

Applicants' Amendment and Response, filed 10/21/05, has been entered. Claims 14 and 15 are amended; claims 14-17 are pending and under current examination.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application No. 10/443,663. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to genetically engineered pluripotent embryonic-like stem cells, and methods of producing the same. The '663 claims are directed to genetically engineered pluripotent embryonic-like stem cells. The instant claims are directed to isolated pluripotent embryonic-like stem cells, which are derived from non-embryonic or postnatal animal cells or tissues, capable of self-renewal and capable to differentiation to cells of all endodermal, ectodermal, and mesodermal lineages, and do not give rise to functional gametes. The instant claims differ from the '663 claims in that they recite that the cells do not give rise to functional gametes. However, the instant claims are rendered obvious by the '663 claims, because they are both directed to the same types of cells, and methods of producing the same, and that the instantly claimed cells encompass cells with the same function (*i.e.*, not giving rise to functional gametes) as claimed in the '663 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 14-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application No. 11/029,763. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to genetically engineered pluripotent embryonic-like stem cells, and methods of producing the same. The '763 claims are directed to genetically engineered pluripotent embryonic-like stem cells. The instant claims are directed to isolated pluripotent embryonic-like stem cells, which are derived from non-embryonic or postnatal animal cells or tissues, capable of self-renewal and capable

to differentiation to cells of all endodermal, ectodermal, and mesodermal lineages, and do not give rise to functional gametes. The instant claims differ from the '763 claims in that they recite that the cells do not give rise to functional gametes. However, the instant claims are rendered obvious by the '763 claims, because they are both directed to the same types of cells, and methods of producing the same, and that the instantly claimed cells encompass cells with the same function (*i.e.*, not giving rise to functional gametes) as claimed in the '763 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". This rejection is maintained for reasons of record, advanced in the prior Office action, mailed 4/19/05, pages 2-4.

*Applicants' Arguments.* Applicants disagree with the prior rejection and submit that the specification enables the skilled artisan to make and use the claimed invention, and that the instantly filed specification provides support for

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pluripotent embryonic-like stem cells, which do not give rise to functional gametes. Applicants point to page 3, lines 29-31 of the specification, for the definition of "totipotent", which means that such cell(s) give rise to all somatic lineages, including functional gametes. This, Applicants argue, provide a distinction between totipotent cells and pluripotent cells, which are instantly claimed; particularly, because pluripotent cells are not totipotent cells, and they cannot form functional gametes (*emphasis in the original*). Applicants argue that nowhere in the specification does it state or suggest that the pluripotent embryonic-like stem cells of the instant invention will form gametes, and that the specification only states that these cells can form somatic cells, and are thus, pluripotent. Applicants argue that they have attempted unsuccessfully to identify the formation of gametes in the pluripotent embryonic-like stem cells of this invention. See pages 4-5 of the Response.

*Response to Arguments.* These arguments have been fully considered, but are not persuasive. The arguments of counsel cannot take the place of evidence in the record. See *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and MPEP §716.01. Applicants have not provided an appropriate affidavit or declaration supporting that the instantly claimed cells cannot give rise to functional gametes. Furthermore, simply pointing to the definition of the term "totipotent" does not provide support that the instantly claimed pluripotent stem cells will not form gametes. The specification is silent with regard to the formation of gametes using the instantly claimed cells. Although Applicants point to the specification for the definition of totipotent, but only in the context of a totipotent zygote. A totipotent cell is one with unlimited capacity that can differentiate, not only into the three germ layers, but produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. The Examiner provides this definition from the NIH website (National Institutes of Health, Resource for Stem

Cell Research [online]. Retrieved on 1/5/06. Retrieved from the Internet:<URL: <http://stemcells.nih.gov/info/scireport/appendixF.asp>> Appendix F).

The specification describes pluripotent embryonic-like stem cells, in that they can differentiate into cells of endodermal, ectodermal and mesodermal lineages (see page 9); however, there is no support for the amendment because the specification does not support that these pluripotent embryonic-like stem cells do not give rise to functional gametes. In fact, the art supports that pluripotent stem cells can, or cannot, give rise to gametes. For example, Piedrahita *et al.* [Biol. Of Reprod., 58:1321-1329 (1998), cited in the prior Office actions] teach the production of porcine chimeras, using primordial germ cells, which are pluripotent cells. Chimeric animals, by definition, have some cells have cells that are contributed by the donor cells, and some from the cells of the recipient blastocysts. Thus, it is possible that a pluripotent stem cell can contribute to the germ line, or it does not, for example, becoming another cell type, such as a neural cell. The instant specification fails to support this amendment, because it does not support that the instantly claimed cells do not form functional gametes.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 14-17 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

### ***Claim Rejections - 35 USC § 112***

The prior rejection of claims 14-17 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicants' amendments to the claims.

***Claim Rejections - 35 USC § 102***

The prior rejection of claims 14-17, under 35 U.S.C. 102(b) as being anticipated by Povey *et al.*, is withdrawn in view of Applicants' amendment to the claims, which now require that the pluripotent embryonic-like stem cell differentiate to cells derived from all of the endodermal, ectodermal, and mesodermal lineages; Povey *et al.* teach hematopoietic stem cells, which are mesodermal cells.

The prior rejection of claims 14-17 under 35 U.S.C. 102(b) as being anticipated by Verma *et al.* is withdrawn in view of Applicants' amendment to the claims, which now require that the pluripotent embryonic-like stem cell differentiate to cells derived from all of the endodermal, ectodermal, and mesodermal lineages; Verma *et al.* teach hematopoietic stem cells, which are mesodermal cells.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Capecchi *et al.* [**Scientific American**, 270(3):34-41 (1994)]. This rejection is maintained for reasons of record, advanced in the prior Office actions, mailed 4/19/05 (pages 5-6) and 10/19/04 (pages 3-5).

*Applicants' Arguments.* Applicants argue that Capecchi do not teach the claimed invention, because they teach mouse ES cells – and these differ as a product, as well as being isolatable from a non-embryonic or postnatal cell (*i.e.*,

made by a different process). Applicants agree that ES cells can, and often do give rise to gametes; however, the nature and limited efficiency of generating transgenic animals from ES cells results in some animals with gamete transmission, and others that do not have gamete transmission. Applicants argue that the important distinction is that totipotent cells, including ES cells, can give rise to gametes, whereas the pluripotent cells of Applicants cannot. Applicants argue that Capecchi's requirement to screen for chimeric mice is as much a function and fact of the overall inefficiency of the process of genetic manipulation and generation of transgenic mice per se, as it is a reflection of the percentage, on a cell by cell basis of totipotent ES cells which may become gametes. Applicants argue that the instantly claimed cells are not anticipated by Capecchi, because they are pluripotent and cannot form gametes. See page 6 of the Response.

*Response to arguments.* These arguments have been fully considered, but are not persuasive. Although Capecchi's cells are isolated from a different source, they fulfill the limitations of the claims because they are transfected, isolated, pluripotent cells which can differentiate into cells derived from all three germ layers, and do not give rise to functional gametes. The NIH stem cell information (cited above) provides a definition for pluripotent cells, which states that, they are cells which have the capability of developing cells from all germ layers. The ES cells taught by Capecchi do not fulfill the definition of "totipotent" stem cells, because they cannot produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs.

The claims state that the cells are "derived from non-embryonic or postnatal animal cells or tissues." However, this requirement is a product made by a particular process. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See

In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Thus, because Capecchi teach cells that are pluripotent, by Applicants' definition, they anticipate the claims.

With regard to Applicants' arguments that the instantly claimed cells cannot give rise to functional gametes, it is noted that the claims require only a single cell that does not give rise to functional gametes. Capecchi teach that the mouse ES cells are used to produce chimeric, transgenic mice. Thus, when a mouse ES cell is injected into a blastocyst, it can form cells that populate the germ line (and can give rise to functional gametes), or it can become a different cell type – such as a neural cell, for example. The evidence that chimeric mice are produced shows that these cells may not give rise to functional gametes. Thus, these teachings produce a cell that fulfills the limitations of the claims.

Capecchi teach the inactivation of target genes by homologous recombination, and the insertion of a *neo* resistance gene, which serves as a positive selection marker in mouse ES cells. See Figure, p. 36. They teach that the ES cells are then cultured and grown into surrogate mothers to generate chimeric mice. See p. 38, Figure. Note that the claimed cells are not distinguished from those taught by Capecchi. Capecchi fulfills the limitations of the claims (the differentiation to cells

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of any endodermal, ectodermal, mesodermal lineage) by showing the generation of mice; further, the methods of producing the genetically engineered cells are also anticipated by Capecchi because they teach transfection of pluripotent embryonic-like stem cells. Accordingly, Capecchi anticipate the claims.

Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Piedrahita *et al.* This rejection is maintained for reasons of record, advanced in the prior Office action mailed 4/19/05 (pages 9-10).

*Applicants' Arguments.* Applicants argue that Piedrahita *et al.* do not anticipate the claimed invention, because they teach that chimeric cells contributed to the germ line. Applicants cite Piedrahita *et al.* to show that ES cells, EG cells and PGCs can have the ability or capability to colonize the germ line following injection in to a host blastocyst. Applicants argue that this contribution to the germ line necessitates the ability to form gametes, and that thus, the PGCs, as taught by Piedrahita *et al.* are in fact, totipotent, and not pluripotent. Applicants argue that because the instantly claimed invention is directed to pluripotent cells which do not produce functional gametes, the invention is not anticipated by Piedrahita *et al.* See page 8 of the Response.

*Response to Arguments.* These arguments are fully considered, but not persuasive. As stated above, totipotent cells are those which produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Piedrahita's cells are considered pluripotent. Furthermore, although pluripotent cells have the ability to colonize the germline (as stated by Piedrahita, and cited by Applicants), the cells also have the ability to differentiate to other cells, as evidenced by the production of chimeric animals. For example, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. It is reiterated that the claims only require a single cell that does not give rise to functional gametes, and this limitation is fulfilled by the teachings of Piedrahita *et*

*al.* Furthermore, as stated above and previously, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the PGCs taught by Piedrahita *et al.*

Piedrahita teach the generation of transgenic porcine chimeras using primordial germ cells (PGCs)-derived colonies. In particular, they teach the isolation of the PGCs from 25-27 day old pig fetuses, (p. 1321, 2<sup>nd</sup> column, Methods & Materials), they show the ability of the PGC to survive and proliferate in an undifferentiated state (see p. 1322, 1<sup>st</sup> column, AP Staining), the ability of the PGCs to differentiate into embryoid bodies (p. 1322, 1<sup>st</sup> column), the transformation of PGCs by electroporation using a plasmid that contained humanized GFP (p. 1322, col. 1-2) and the generation of chimeric pig fetuses and pigs using the transformed PGCs.

Piedrahita *et al.* anticipate the claimed invention because the PGCs they teach are capable of differentiation into the three germ layers (as evidenced by both the generation of embryoid bodies and the generation of chimeric pig fetuses and chimeric piglets). Chimeric animals, by definition, have some cells have cells that are contributed by the donor cells, and some from the cells of the recipient blastocysts. Piedrahita teach the analysis of transgene expression and show that the pigs expressed the transgene in different tissues, they teach that analysis of the developing fetuses suggests that although some may have germ line transmission, it would require that the chimeric cells contribute to the germ line. See p. 1328, 2<sup>nd</sup> column, 2<sup>nd</sup> full ¶, and p. 1329, 1<sup>st</sup> column, 2<sup>nd</sup> ¶. Accordingly, Piedrahita anticipate the claimed invention.

### ***Claim Rejections - 35 USC § 103***

The prior rejection of claims 14-17 under 35 U.S.C. 103(a) as being unpatentable over Pittenger *et al.* in view of Sambrook *et al.* is withdrawn in view

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of Applicants' amendment to the claims, which now require that the pluripotent embryonic-like stem cell differentiate to cells derived from all of the endodermal, ectodermal, and mesodermal lineages; Pittenger *et al.* only teach mesenchymal stem cells, thus, the combination of the references does not teach or suggest the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamblott when taken with Sambrook *et al.* This rejection is maintained for reasons of record, advanced on pages 13-15 of the Office action, mailed 4/19/05; pages 9-11 of the Office action, mailed 10/19/04.

*Applicants' Arguments.* Applicants argue that, as noted above, with regard to Piedrahita *et al.*, that the PGCs taught by Shamblott are totipotent, not

pluripotent cells, because Shamblott teaches that germ-line transmission can be achieved in chimeric animals. Thus, Applicants argue that the PGCs of Shamblott are similar to ES cells, and can form gametes to demonstrate germ-line transmission. Applicants argue that this distinguishes that instantly claimed cells from that of the combined teachings of Shamblott and Sambrook *et al.* See pages 9-10 of the Response.

*Response to Arguments.* These arguments are fully considered, but are not persuasive. As stated above, the cells of Shamblott are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Furthermore, although pluripotent cells have the ability to colonize the germline (as stated by Shamblott, and cited by Applicants), the cells also have the ability to differentiate to other cells, as evidenced by the production of chimeric animals. For example, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. It is reiterated that the claims only require a single cell that does not give rise to functional gametes, and this limitation is fulfilled by the combined teachings of Shamblott and Sambrook *et al.* Furthermore, as stated above and previously, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the PGCs taught by Shamblott. Shamblott teaches that the PGCs are pluripotent, as are the claimed cells. The specification teaches that a pluripotent stem cell is capable of self-regeneration, differentiation to cells of endodermal, ectodermal and mesodermal lineages (see p. 35-36).

Shamblott *et al.* teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells [PGCs] and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers [see *Abstract*]. In particular, Shamblott *et al.* teach that gonadal ridges and

mesenteries of 5 to 9 week old human fetuses and cells initially cultured on a layer of mouse STO fibroblast feeder layer. The cells formed embryoid bodies, which were collected and analyzed immunohistochemically [see pp. 13726-13727, *Materials & Methods*]. It was found that the embryoid bodies demonstrated derivatives of the three embryonic germ layers [see p. 13729, 2<sup>nd</sup> column and Table 1]. Note that Shamblott teach the pluripotent embryonic-like stem cells because the claims do not provide any requisite characteristics (*e.g.*, specific markers, etc.) of the claimed embryonic-like stem cells such that they would be distinguished from the cells taught by Shamblott. The claims recite that the embryonic-like stem cells are "derived from non-embryonic or postnatal animal cells or tissue;" however, this recitation does not differentiate them from the cells as taught by Shamblott. Further, the method claim has been included in this rejection because the cells as instantly claimed are not distinguishable from those taught in the art. The cells as taught by Shamblott fulfill the requirements of the claims because they are capable of differentiation to cells of each and any of endodermal, ectodermal and mesodermal lineages, and are capable of self-renewal.

Shamblott do not teach the transfection of the pluripotent stem cells to produce a genetically engineered pluripotent stem cell. However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Shamblott and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the PGCs, as taught by Shamblott and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or

to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson when taken with Sambrook *et al.* This rejection is maintained for reasons of record advanced on pages 16-17 of the Office action, mailed 4/19/05; pages 12-13 of the Office action, mailed 10/19/04.

*Applicants' Arguments.* Applicants' argue, as above, that the instantly claimed cells are distinct and unobvious from the instantly claimed cells, because Thomson's cells are totipotent cells, and the cells of the instant invention are pluripotent and do not give rise to functional gametes. See p. 10-11 of the Response.

*Response to Arguments.* This is not found to be persuasive. As stated above, the cells of Thomson are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Furthermore, although pluripotent cells have the ability/capability to colonize the germline, pluripotent cells also have the ability to differentiate to other cells, as evidenced by the production of chimeric animals. For example, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. It is reiterated that the claims only require one cell that does not give rise to functional gametes, and this limitation is fulfilled by the combined teachings of Thomson and Sambrook *et al.*

Furthermore, the instantly claimed cells are not found to be distinguished by that of the art because there are no requisite characteristics that differentiate them from, for example, the pluripotent cells, as taught by Thomson. Thomson teaches that the isolated cells are pluripotent, as are the claimed cells. The specification

teaches that a pluripotent stem cell is capable of self-regeneration, differentiation to cells of endodermal, ectodermal and mesodermal lineages (see p. 35-36).

Thomson teach the isolation of ES cells from the rhesus monkey. See p. 7844, *Materials and Methods*, col. 2. The cells are capable of maintaining an undifferentiated state and proliferate indefinitely, and have the potential to differentiate into derivatives of all three embryonic germ layers. They teach that the cells differentiated into cells of endoderm, mesoderm and ectoderm. See *Abstract* and p. 7846, col. 1-2, bridging ¶. Note that the claims fail to distinguish the claimed cells from the cells taught by Thomson. Thus, the method claim has been included in the rejection because the cells used in the method are not distinguished from those taught by Thomson. Thomson do not teach that the ES cells are genetically engineered to express a gene or protein of interest.

However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Thomson and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the pluripotent embryonic stem cells, as taught by Thomson and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

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*Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

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Thaian N. Ton  
Patent Examiner  
Group 1632